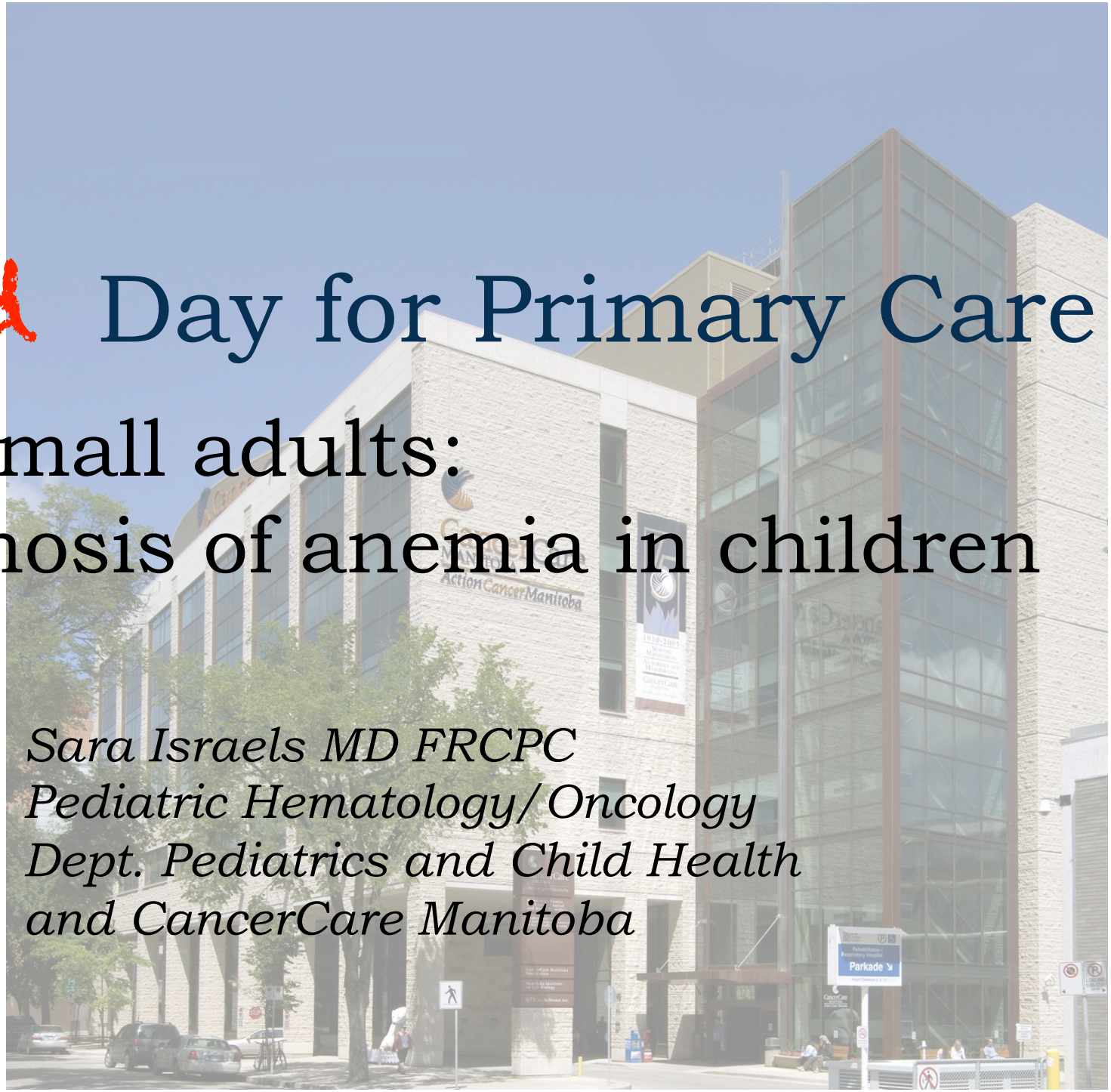
CancerCare Manitoba

Blood Day for Primary Care

Not small adults: Diagnosis of anemia in children



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UPCON
Uniting Primary Care and Oncology

University of Manitoba

Disclosures

1. No disclosures relevant to this presentation

Objectives

At the completion of this talk you will be aware that:

1. The definition of anemia is age-dependent
2. The causes of anemia differ in frequency across the age continuum
3. Congenital causes of anemia should be considered when investigating children

Referral to Pediatric Hematology

"Dear Pediatric Hematologist:

Please see this 20 month old boy for investigation of persistent anemia: HGB 107 g/L, MCV 72 fL."

Does this child have anemia?

a) YES

b) NO

c) NOT SURE

Age	HGB g/L Mean	HGB g/L -2SD	MCV fL Mean	MCV fL -2SD
FT Newborn	165	135	108	98
1-3 days	185	145	108	95
2 weeks	166	134	105	88
1 month	139	107	101	91
6 months	126	111	76	68
6 mo-2 yrs	120	105	78	70
2-6 years	125	115	81	75
6-12 years	135	115	86	77
12-18 years (M) (F)	 145 140	 130 120	 88 90	 78 78
Adults (M) (F)	 155 140	 135 120	 90 90	 80 80

Tip #1: Age-dependent reference ranges

- Normal ranges for hemoglobin, hematocrit, and RBC indices (other CBC parameter, too) are age-dependent from infancy to late teen years.

- Does your laboratory provide you with age-dependent reference ranges on the CBC report?

Is it just anemia?

- Are other cell lines normal, or are you actually dealing with more than one cytopenia?
  - Anemia and thrombocytopenia
  - Anemia and neutropenia
  - Pancytopenia

Tip #2: Be alert to multiple cytopenias

- The differential diagnosis of multiple cytopenias is not the same as for isolated anemia: investigations may be different, particularly if the child is acutely ill.

Tip #3: Know what is common in children

- CBC, RBC indices and reticulocyte count are the most useful initial tests.
- The frequency of specific diagnoses differ from adults and by age, gender and ethnic background.
- Frequency:

microcytic anemias >> normocytic anemias>> macrocytic anemias

Referral to Pediatric Hematology

"Dear Pediatric Hematologist:

Please see this 13 year old girl with chronic Fe deficiency anemia. Hb 108-110, indices suggest iron deficiency.

Irregular periods. Has been on iron supplementation for three months, but not compliant. May have an eating disorder.

Mother died of colon cancer at age 29 years.

Unable to obtain stool O.B. on daughter."

Referral to Pediatric Hematology

	Patient	Ref. Range
WBC x 10^9/L	7.34	5.0-15.0
HGB (g/L)	109	120-160
RBC x 10^{12}/L	5.34	4.1-5.3
MCV (fL)	65	80-98
MCH (pg)	20.4	25-35
RDW (%)	17.3	11.4-14.4
Retic. x 10^9/L	59	20-75
Platelets x 10^9/L	240	150-500
Blood film	microcytosis, anisocytosis	
Ferritin (ug/L)	45	20-140

What is the most likely cause of anemia in this girl?

1. Iron deficiency anemia
2. Anemia of chronic disease
3. Thalassemia trait
4. Folate deficiency

Referral to Pediatric Hematology

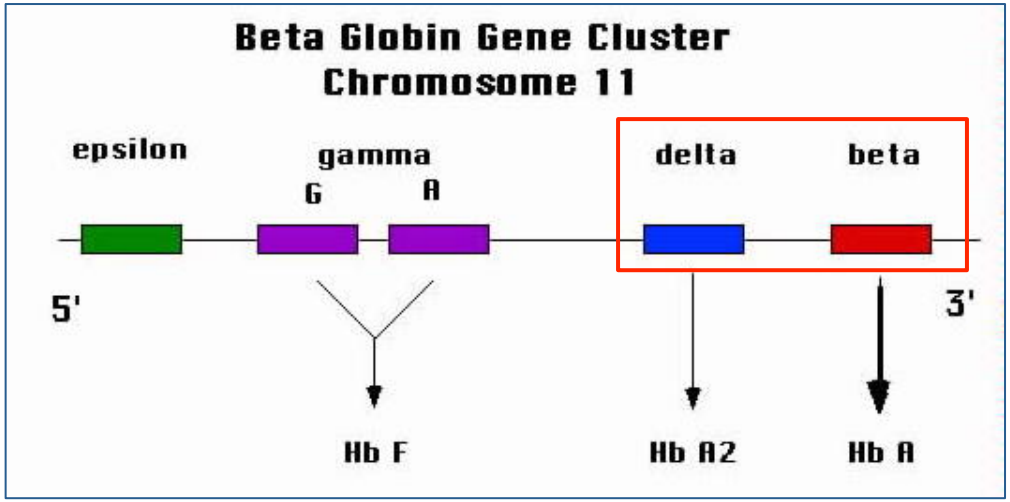
Hgb electrophoresis

Hgb A	90.2%	(96-98%)
Hgb F	7.2%	(<0.5%)
Hgb A_2	2.6%	(2.1-3.2%)

Molecular studies

Heterozygous for a partial deletion of the beta-globin gene cluster, removing the delta and beta genes.

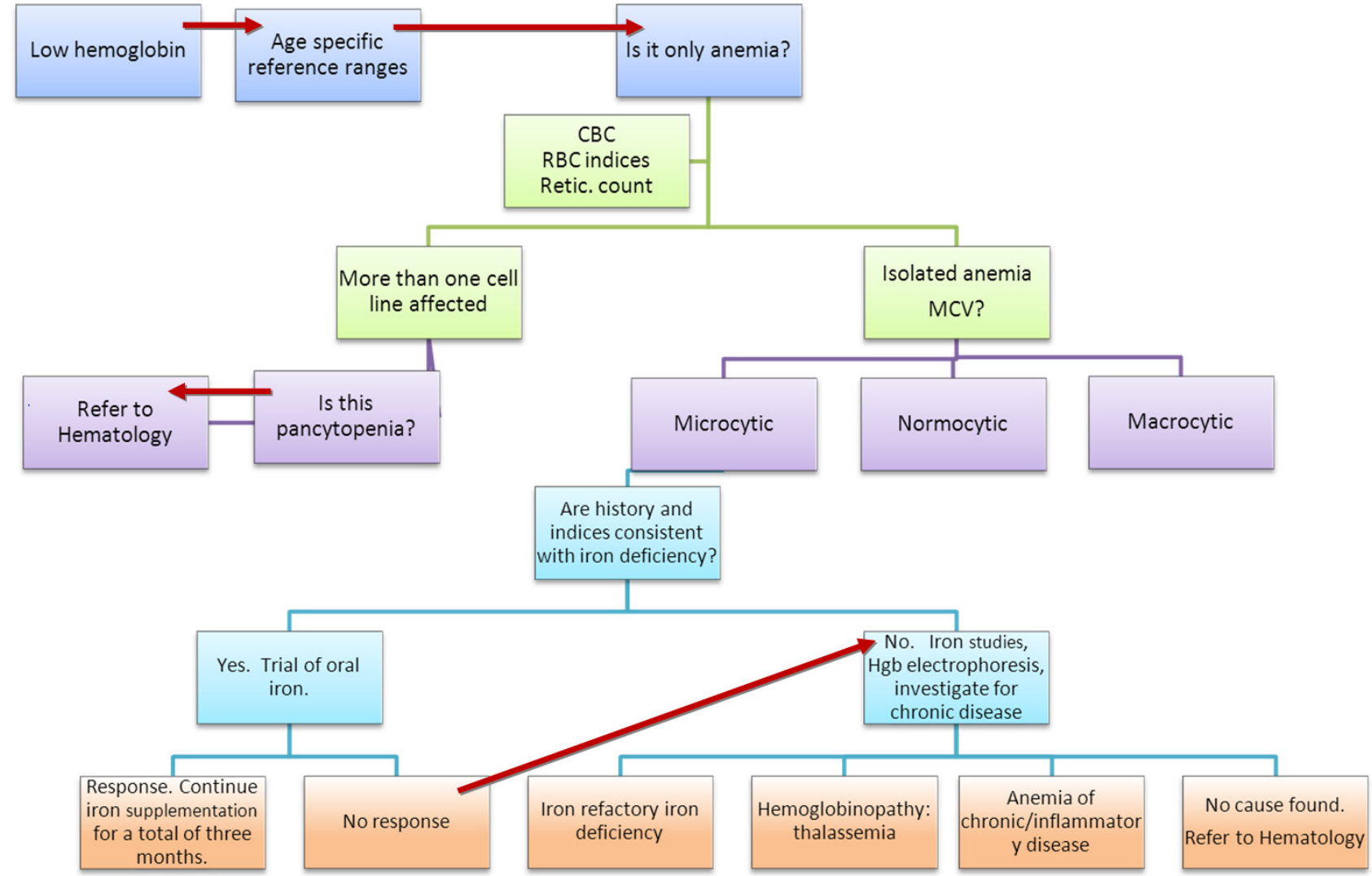
Dx: Delta-beta thalassemia



Tip #4: Microcytic anemia is not always iron deficiency

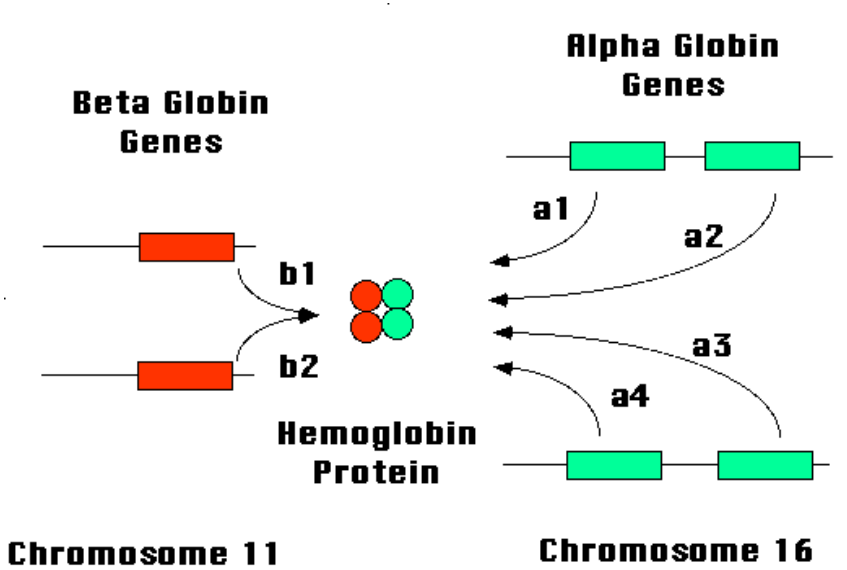
- Microcytic anemias are common
- Iron deficiency may be the most common diagnosis but not the only diagnosis
- RBC count, RBC indices, Reticulocyte count and blood film provided additional information.
- A limited trial of oral iron (1 month) is reasonable if age, history and laboratory screening support iron deficiency as the most likely diagnosis. If there is an inadequate response, broaden the differential diagnosis

Work-up of MICROCYTIC ANEMIA in CHILDREN



Tip #5: Microcytic anemia: is it thalassemia?

- The prevalence of alpha and beta thalassemia syndromes is increasing, as demographics shift in Manitoba.
- Hemoglobin electrophoresis is most useful when patient is not also iron deficient.
- Why confirm the diagnosis?
  - Avoid prolonged iron therapy
  - Genetic counseling



http://sickle.bwh.harvard.edu/thal_inheritance.html

Referral to Pediatric Hematology

"Dear Pediatric Hematologist:

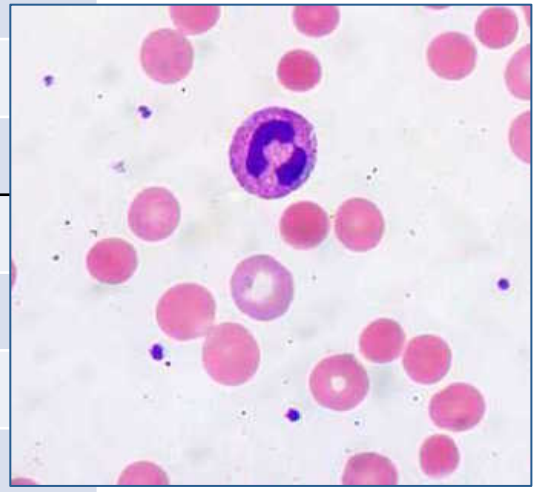
Please see this 3 year old girl with three documented episodes of sudden worsening of anemia and jaundice, associated with progressive splenomegaly. Anemia has responded to courses of prednisone, but spleen continues to enlarge.

She had prolonged neonatal jaundice, treated with phototherapy. She has been on iron supplementation for 3 years.

On examination, is pale and jaundiced. Her spleen is palpable 6 cm below left costal margin."

Referral to Pediatric Hematology

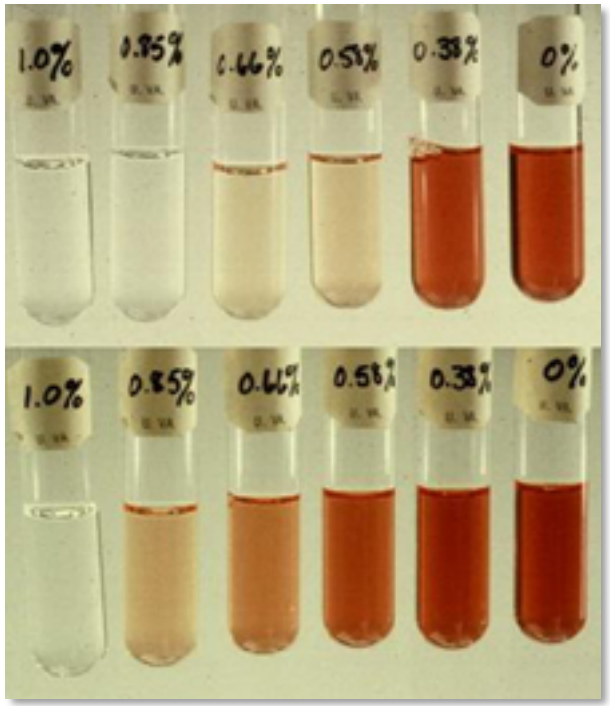
	Patient	Ref. Range
WBC x 10^9/L	9.5	5.0-15.0
HGB (g/L)	77	115-135
RBC x 10^{12}/L	2.8	3.9-5.3
MCV (fL)	78	75-87
RDW (%)	30.3	11.4-14.4
Retic. x 10^9/L	307	20-75
Platelets x 10^9/L	330	150-500
LDH (U/L)	643	190-400
Bilirubin (mmol/L)	185	3-18
Ferritin (ug/L)	247	21-310
DAT	negative	



What is the most likely cause of this girl's anemia?

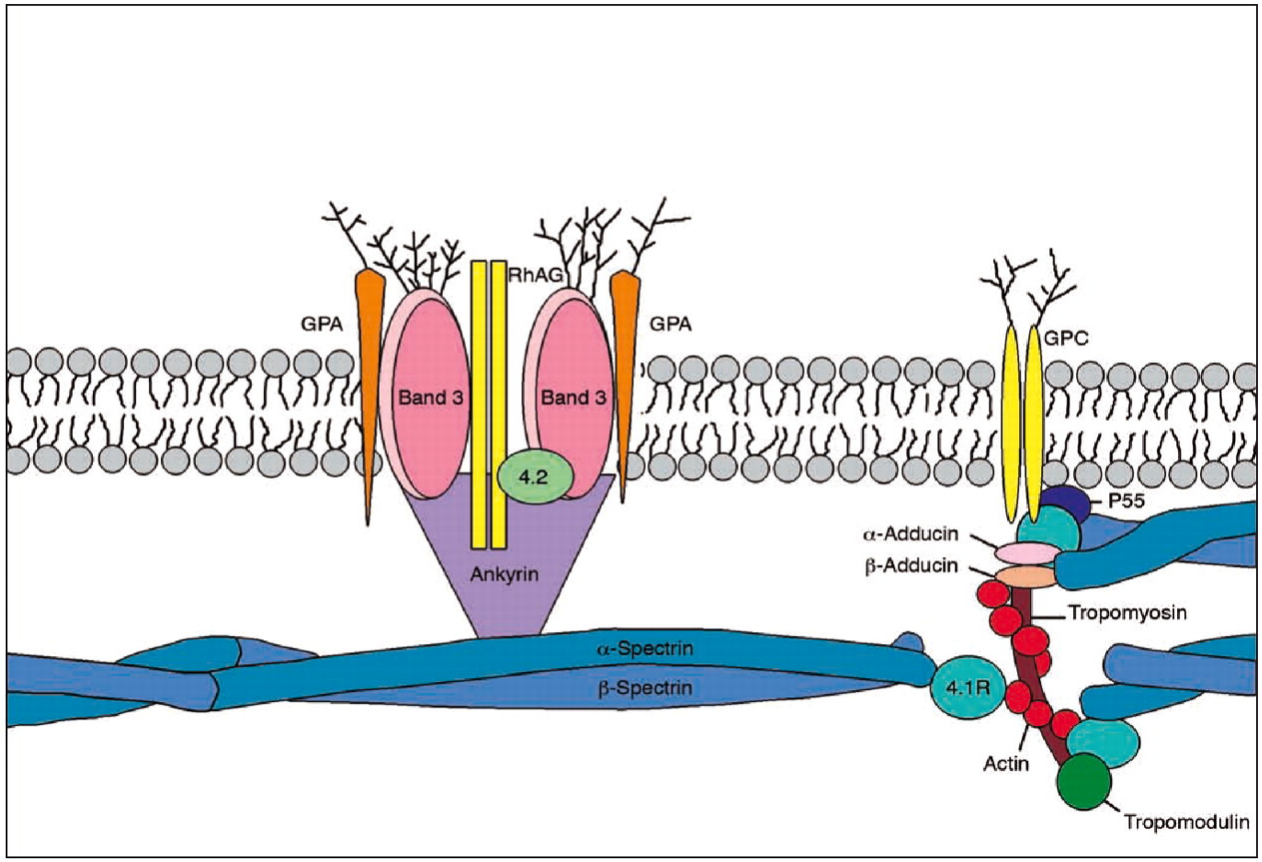
1. Autoimmune hemolytic anemia
2. Hereditary spherocytosis
3. Anemia of chronic inflammation
4. Drug-induced hemolysis

Referral to Pediatric Hematology



- RBC osmotic fragility: increased
  - Dx: Hereditary spherocytosis
  - Sensitivity 85%
- EMA-binding test: Flow cytometric method using a fluorescent probe, eosin-5'-maleimide, which binds to protein band 3 complex.
  - Sensitivity 95%

Hereditary Spherocytosis

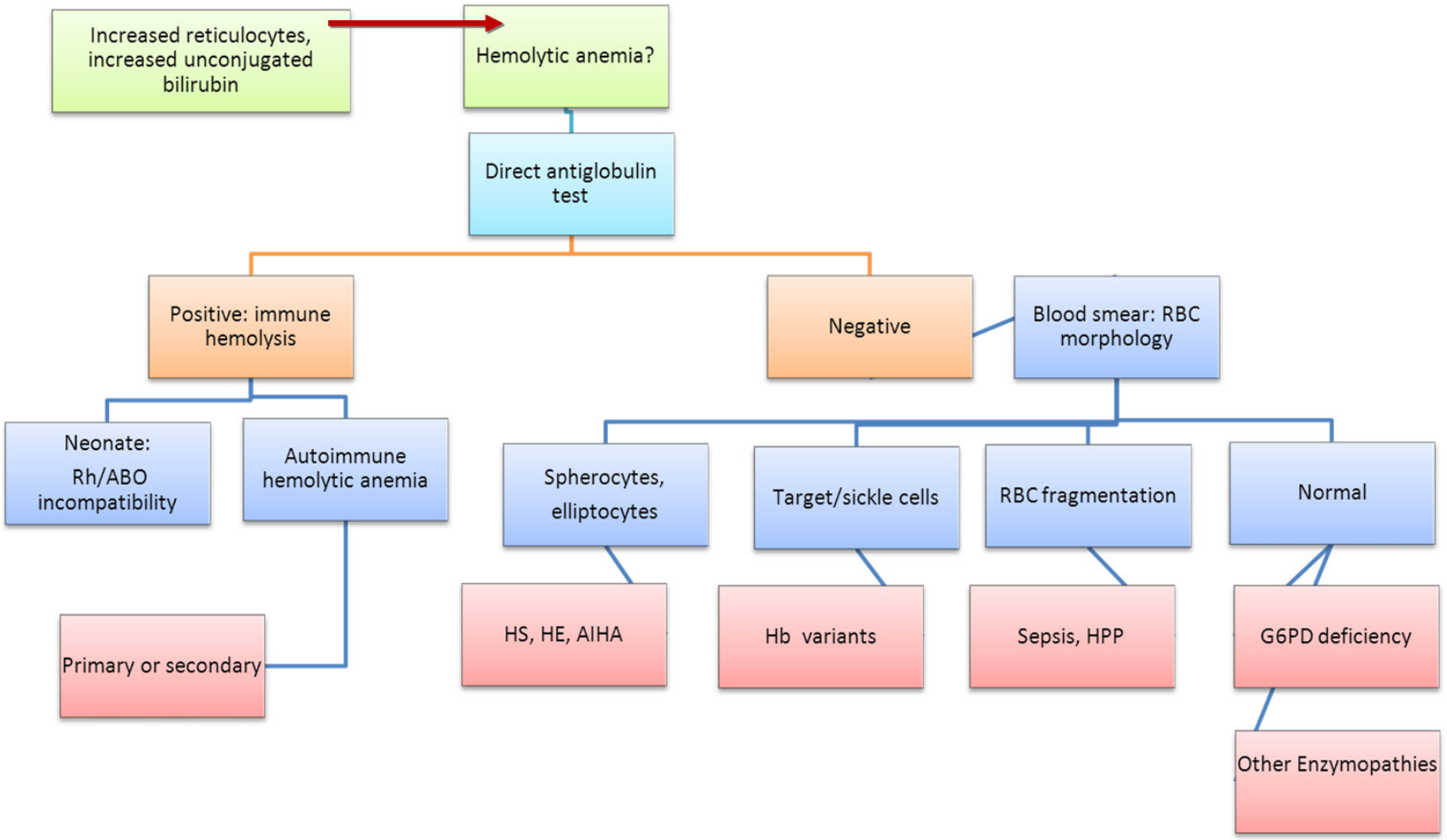


Haematologica September 200893:1283-1288

Tip #6: Consider congenital hemolytic anemia

- In addition to the CBC, reticulocyte count, bilirubin and review of the blood smear are the most useful tests.
- Hemolytic anemias in children are often congenital/hereditary. Clues to a congenital hemolytic anemia:
  - Direct antiglobulin test: negative
  - Prolonged or severe neonatal jaundice
  - Exacerbation by inter-current viral illnesses
  - Progressive splenomegaly
- Transient bone marrow hypoplasia may cause dramatic fall in Hgb and reticulocyte count

Work-up of HEMOLYTIC ANEMIAS in CHILDREN



Neonates are a special case

Work-up of NEONATAL ANEMIAS

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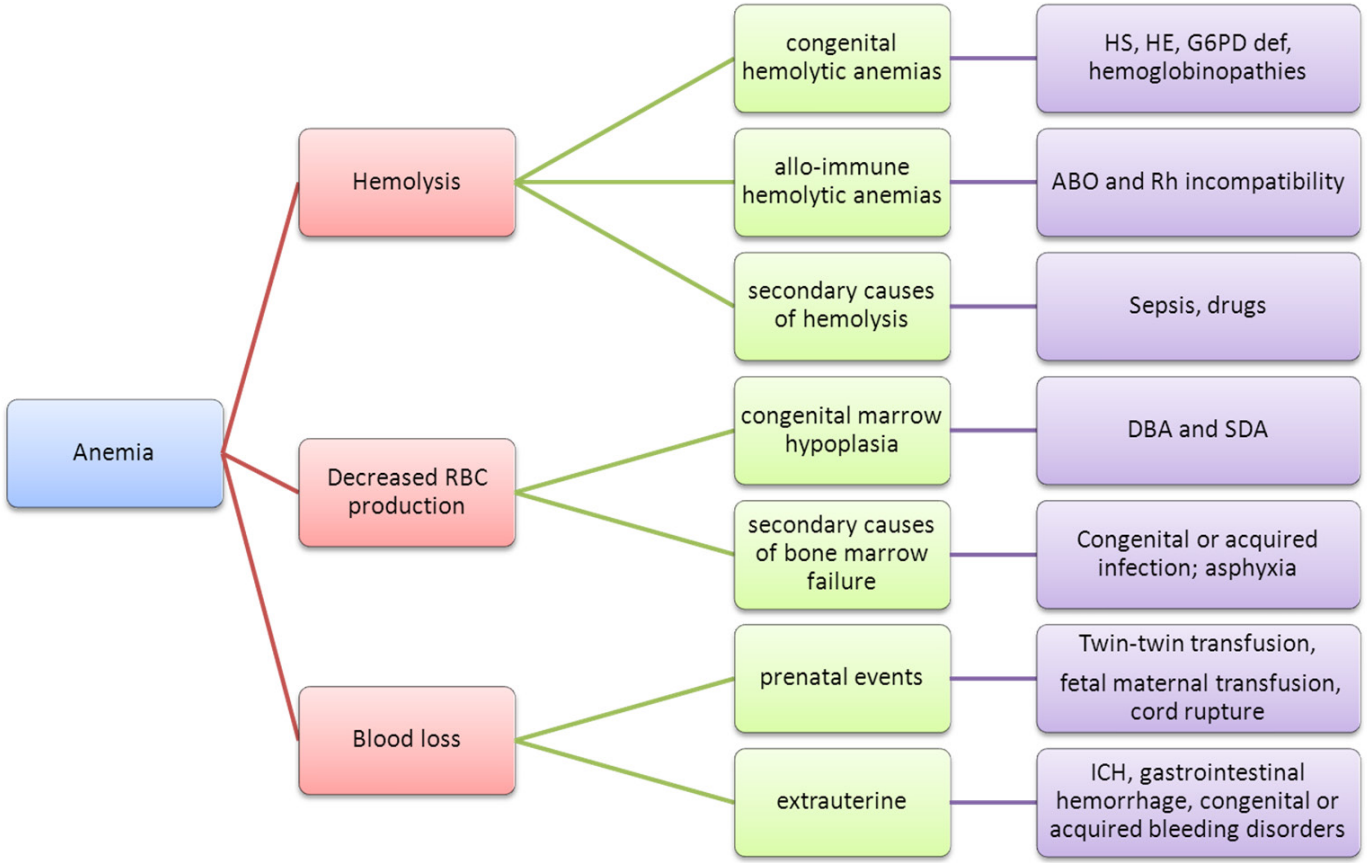

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Pathways are subject to clinical judgment and actual practice patterns may not always follow the proposed steps in this pathway.

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When to consider referral to Pediatric Hematology

- Cytopenias affecting more than one cell line
- RBC parameters suggesting bone marrow hypofunction/failure: decreased reticulocyte count, normocytic/macrocytic indices
- Persistent anemia severe enough consider transfusion
- Iron refractory iron deficiency anemia
- When you are concerned, please call us. We can often make some initial recommendations by phone

Key points:

1. Use age-dependent normal ranges when considering CBC results in a child.
2. Microcytic anemias are common in childhood. Consider alternative etiologies to iron deficiency, including hemoglobinopathies.
3. Congenital/hereditary causes of anemia deserve consideration in all anemia evaluations in children.

A useful reference

Practical Algorithms in Pediatric Hematology/Oncology (Sills, Ed.):

http://www.scribd.com/doc/115231629/Practical-Algorithms-in-Pediatric-Hematology-and-Oncology#scribd

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